

What Is Claimed Is:

1. A method for predicting a hypoglycemic event in a subject, said method  
5 comprising,  
determining (i) a threshold glucose value that corresponds to said  
hypoglycemic event, and (ii) at least one threshold parameter value that is correlated  
with said hypoglycemic event, wherein the parameter is either skin conductance  
readings or temperature readings,  
10 obtaining a series of glucose measurement values at selected time intervals  
using a method comprising  
extracting a sample comprising glucose from the subject using  
a transdermal sampling system that is in operative contact with a skin  
or mucosal surface of said subject;  
15 obtaining a raw signal from the extracted glucose, wherein said  
raw signal is specifically related to glucose amount or concentration in  
the subject;  
correlating the raw signal with a glucose measurement value  
indicative of the amount or concentration of glucose present in the  
20 subject at the time of extraction;  
repeating said extracting, obtaining, and correlating to provide a  
series of measurement values at selected time intervals, wherein the  
sampling system is maintained in operative contact with the skin or  
mucosal surface of said subject during said extracting, obtaining, and  
25 correlating to provide for frequent glucose measurements;  
predicting a measurement value at a further time interval  
subsequent to said series of measurement values, said further time  
interval represented as  $n+1$ ; and  
comparing said predicted measurement value to said threshold  
30 glucose value, wherein a measurement value lower than the threshold

value is designated to be hypoglycemic;

measuring a parameter value or trend of parameter values concurrently,  
simultaneously, or sequentially with said obtaining of the series of measurement  
values, wherein the parameter value or trend of parameter values is reflective of either  
5 skin conductance readings or temperature readings of the subject, and comparing said  
parameter value or trend of parameter values with said threshold parameter value to  
determine whether said parameter value or trend of parameter values indicates a  
hypoglycemic event; and

predicting a hypoglycemic event in said subject when both (i) comparing said  
10 predicted measurement value to said threshold glucose value indicates a  
hypoglycemic event at time interval  $n+1$ , and (ii) comparing said parameter with said  
threshold parameter value indicates a hypoglycemic event.

2. The method of claim 1, wherein the selected time intervals are evenly  
15 spaced.

3. The method of claim 1, wherein the series of measurement values  
comprises three or more discrete values.

4. The method of claim 3, wherein the further time interval  $n+1$  occurs one  
20 time interval after the series of measurement values.

5. The method of claim 1, wherein both skin conductance readings and  
temperature readings are used to predict the likelihood of a hypoglycemic event at  
25 time interval  $n+1$ .

6. The method of claim 3, wherein said predicting of the measurement value  
at a further time interval is carried out using said series of three or more measurement  
values in a series function represented by:

$$y_{n+1} = y_n + \alpha(y_n - y_{n-1}) + \frac{\alpha^2}{2}(y_n - 2y_{n-1} + y_{n-2}) \quad (7)$$

wherein  $y$  is the measurement value of glucose,  $n$  is the time interval between measurement values, and  $\alpha$  is a real number between 0 and 1.

5           7. The method of claim 6, wherein the series function is used to predict the value of  $y_{n+1}$  and the time interval  $n+1$  occurs one time interval after the series of measurement values is obtained.

10           8. The method of claim 1, wherein said sampling system comprises a sweat probe and said skin conductance readings are obtained using said sweat probe.

15           9. The method of claim 1, wherein said sampling system comprises a temperature probe and said temperature readings are obtained using said temperature probe.

20           10. The method of claim 1, wherein said sample is extracted from the subject into one or more collection reservoir to obtain an amount or concentration of glucose in a reservoir.

25           11. The method of claim 10, wherein the one or more collection reservoirs are in contact with the skin or mucosal surface of the subject and the sample is extracted using an iontophoretic current applied to said skin or mucosal surface.

            12. The method of claim 11, wherein at least one collection reservoir comprises an enzyme that reacts with the extracted glucose to produce an electrochemically detectable signal.

            13. The method of claim 11, wherein said enzyme is glucose oxidase.

14. The method of claim 1, wherein said obtaining of the series of glucose measurement values is performed using a near-IR spectrometer.

15. A glucose monitoring system for measuring glucose in a subject, said  
5 system comprising, in operative combination:

a sensing mechanism in operative contact with the subject or with a glucose-containing sample extracted from the subject, wherein said sensing mechanism obtains a raw signal specifically related to glucose amount or concentration in the subject;

10 a device to obtain either skin conductance readings or temperature readings from the subject, and

one or more microprocessors in operative communication with the sensing mechanism, wherein said microprocessors comprise programming to (i) control the sensing mechanism to obtain a series of raw signals at selected time intervals, (ii)  
15 correlate the raw signals with measurement values indicative of the amount or concentration of glucose present in the subject to obtain a series of measurement values, (iii) predict a measurement value at a further time interval, which occurs after the series of measurement values is obtained, (iv) compare said predicted measurement value to a predetermined value, wherein a predicted measurement value  
20 lower than the predetermined value is designated to be hypoglycemic, (v) control the device for measuring skin conductance readings or temperature readings of the subject, (vi) compare said skin conductance readings or temperature readings with a threshold parameter value or trend of parameter values to determine whether said skin conductance readings or temperature readings indicate a hypoglycemic event; and  
25 (vii) predict a hypoglycemic event in said subject when both (a) comparing said predicted measurement value to said threshold glucose value indicates a hypoglycemic event at time interval  $n+1$ , and (b) comparing said skin conductance readings or temperature readings with a threshold parameter value or trend of parameter values indicates a hypoglycemic event.

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16. The monitoring system of claim 15, wherein the sensing mechanism comprises a biosensor having an electrochemical sensing element.

5 17. The monitoring system of claim 15, wherein the sensing mechanism comprises a near-IR spectrometer.

18. The monitoring system of claim 15, wherein said device to obtain said skin conductance readings is a sweat probe.

10 19. The monitoring system of claim 15, wherein said device to obtain said temperature readings is a temperature probe.

20. The monitoring system of claim 15, wherein the selected time intervals are evenly spaced.

15 21. The monitoring system of claim 15, wherein the series of measurement values obtained comprises three or more discrete values.

20 22. The monitoring system of claim 21, wherein the further time interval occurs one time interval after the series of measurement values.

23. The monitoring system of claim 15, wherein both skin conductance readings and temperature readings are used to predict the likelihood of a hypoglycemic event at the further time interval.

25 24. The monitoring system of claim 21, wherein said predicting of a measurement value at a further time interval is carried out using said series of three or more measurement values in a series function represented by:

$$y_{n+1} = y_n + \alpha(y_n - y_{n-1}) + \frac{\alpha^2}{2}(y_n - 2y_{n-1} + y_{n-2}) \quad (7)$$

wherein  $y$  is the measurement value of glucose,  $n$  is the time interval between measurement values, and  $\alpha$  is a real number between 0 and 1.

25. The monitoring system of claim 24, wherein the series function is used to  
5 predict the value of  $y_{n+1}$  and the time interval  $n+1$  occurs one time interval after the series of measurement values is obtained.

26. One or more microprocessors, comprising  
programming to control

10 (i) a sensing mechanism to obtain a series of raw signals at selected time intervals, wherein the raw signal is related to an amount or concentration of glucose in a subject, (ii) a device to obtain either a series of skin conductance readings or a series of temperature readings from the subject, (iii) correlating the raw signals with measurement values indicative of the amount or concentration of glucose present in  
15 the subject to obtain a series of glucose measurement values, (iv) predicting a glucose measurement value at a further time interval, which occurs after the series of measurement values is obtained, (v) comparing said predicted measurement value to a predetermined value, wherein a predicted measurement value lower than the predetermined value is designated to be hypoglycemic, (v) controlling the device for  
20 measuring skin conductance readings or temperature readings of the subject, (vi) comparing said skin conductance readings or temperature readings with a threshold parameter value or trend of parameter values to determine whether said skin conductance readings or temperature readings indicate a hypoglycemic event; and  
(vii) predicting a hypoglycemic event in said subject when both (a) comparing said  
25 predicted measurement value to said threshold glucose value indicates a hypoglycemic event at time interval  $n+1$ , and (b) comparing said skin conductance readings or temperature readings with a threshold parameter value or trend of parameter values indicates a hypoglycemic event.

30 27. The one or more microprocessors of claim 26, wherein the sensing

mechanism comprises a biosensor having an electrochemical sensing element.

28. The one or more microprocessors of claim 26, wherein the sensing mechanism comprises a near-IR spectrometer.

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29. The one or more microprocessors of claim 26, wherein the selected time intervals are evenly spaced.

30. The one or more microprocessors of claim 26, wherein the series of measurement values obtained comprises three or more discrete values.

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31. The one or more microprocessors of claim 26, wherein the further time interval occurs one time interval after the series of measurement values.

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32. The one or more microprocessors of claim 26, wherein both skin conductance readings and temperature readings are used to predict the likelihood of a hypoglycemic event at the further time interval.

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33. The one or more microprocessors of claim 30, wherein the predicting a glucose measurement value at a further time interval is carried out using said series of three or more measurement values in a series function represented by:

$$y_{n+1} = y_n + \alpha(y_n - y_{n-1}) + \frac{\alpha^2}{2}(y_n - 2y_{n-1} + y_{n-2}) \quad (7)$$

wherein  $y$  is the measurement value of glucose,  $n$  is the time interval between measurement values, and  $\alpha$  is a real number between 0 and 1.

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34. The one or more microprocessors of claim 33, wherein the series function is used to predict the value of  $y_{n+1}$  and the time interval  $n+1$  occurs one time interval after the series of measurement values is obtained.